

# Notice of Allowability

Application No.

09/448,613

Examiner

Richard Schnizer, Ph. D

Applicant(s)

MCCRAY JR. ET AL.

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## -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to amendment filed 8/12/03.
2. ☐ The allowed claim(s) is/are 1-8, 10-12, 26-37, 48-54, 56, 66 and 70.
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - \* Certified copies not received: \_\_\_\_\_.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
  - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☒ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No. \_\_\_\_\_.
  - (b) ☐ including changes required by the proposed drawing correction filed \_\_\_\_\_, which has been approved by the Examiner.
  - (c) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

### Attachment(s)

- |   |   |
|---|---|
| 1 <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 5 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)          |
| 2 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6 <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____.            |
| 3 <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No. _____  | 7 <input checked="" type="checkbox"/> Examiner's Amendment/Comment                  |
| 4 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
|   | 9 <input type="checkbox"/> Other _____  |

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Steven Highlander on 12/11/03.

The application has been amended as follows:

IN THE CLAIMS:

Replace Claim 1 with the following:

--A method for increasing viral vector infection of epithelial cells in an epithelial tissue comprising:

- a) contacting said epithelial tissue with a composition that comprises a hypotonic solution and/or a chelator of divalent cations in an amount sufficient to produce permeabilized epithelial tissue; and
- b) contacting said permeabilized epithelial tissue with a viral vector;

whereby an increase in transepithelial permeability increases viral vector infection of said epithelial cells.--

In claim 10, delete "tissue permeabilizing agent is" and insert --composition comprises-- therefor.

Replace claim 11 with the following:

--The method of claim 1, wherein said composition comprises a chelator of divalent cations.—

In claim 12 delete "ion chelator" and substitute --chelator of divalent cations-- therefor.

In claim 26, delete ", following the step of increasing transepithelial permeability," and insert --in said permeabilized tissue-- immediately after "epithelial cells".

In claims 36 and 37, delete "tissue permeabilizing agent" and substitute -- composition-- therefor.

In claim 48, delete "A", and substitute --An—therefor, and delete "an ion chelator" and substitute --a chelator of divalent cations-- therefor.

In claim 50 delete "an ion chelator" and substitute --a chelator of divalent cations-- therefor.

In item (c) of claim 50, delete "said epithelial" and insert --the permeabilized epithelial-- therefor.

Replace claim 53 with the following:

--A method of increasing transport of chloride ions in airway epithelial tissue of a mammal suffering from cystic fibrosis comprising:

- a) providing a packaged viral vector comprising a polynucleotide encoding a cystic fibrosis transmembrane regulator (CFTR) protein;
- b) contacting said airway epithelial tissue with a hypotonic solution and/or a chelator of divalent cations in a sufficient amount to produce permeabilized epithelial tissue; and
- c) contacting cells of said permeabilized airway epithelial tissue with said packaged viral vector under conditions permitting uptake of the packaged viral vector by said cells, and expression of said CFTR protein therein;

wherein a sufficient quantity of said CFTR protein is produced to increase chloride ion transport in the airway epithelial tissue.--

### ***Drawings***

The Drawings are objected to because they are not labeled consistently with the Brief Description of the Drawings in the specification.

The Brief Description of the Drawings lists Fig. 2A, 2B, 4A, 4B, 4C, 4D, 5A, 5B, 8A, and 8B, whereas the Drawings depict only a single Fig 2, with 2 panels 'A' and 'B', a single Fig 5 with 4 panels 'A'-'D', etc. This objection can be overcome by submitting new drawings wherein the existing panels are relabeled as Fig. 2A, Fig. 2B, Fig. 4A, Fig. 4B, Fig. 4C, Fig. 4D, Fig. 5A, Fig. 5B, Fig. 8A, and Fig. 8B.

***Reasons for Allowance***

The following is an examiner's statement of reasons for allowance: The claims have been amended to recite "chelator of divalent cations", rather than "ion chelator". The phrase "chelator of divalent cations" more accurately reflects the nature of the invention and is adequately supported by the specification. For example, the specification lists three species of ion chelators (EGTA, BAPTA, and EGTA) each of which is a chelator of divalent cations. Furthermore, divalent cation chelators were well known in the art at the time of the invention, as was the fact that epithelial permeability could be increased by chelating divalent cations such as  $Mg^{2+}$  and  $Ca^{2+}$ . See for example abstracts of Lacaz-Vieira (JOURNAL OF GENERAL PHYSIOLOGY, (1997 Dec) 110 (6) 727-40), Sakoff et al (BIOCHEMICAL AND MOLECULAR MEDICINE, (1996 Apr) 57 (2) 81-90), Cho et al (PHARMACEUTICAL RESEARCH, (1990 Apr) 7 (4) 325-31), and Noach et al (International Journal of Pharmaceutics (1993), 90(3), 229-37).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441 until 1/13/04, and thereafter will be 571-272-0762. The examiner can

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normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at 703-306-3217 before 2/22/04, and at 571-272-0811 after 2/22/04. The official central fax number is 703-872-9306 until further notice. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413 prior to 1/14/04, and thereafter will be 571-272-0564.



DAVE T. NGUYEN  
PRIMARY EXAMINER

Richard Schnizer, Ph.D.

